

YAGFL	(SEQ ID NO.: 5)	YaGFL	(SEQ ID NO.: 20)
YSGFL	(SEQ ID NO.: 6)	YsGFL	(SEQ ID NO.: 21)
LGGFL	(SEQ ID NO.: 7)	YpGFL	(SEQ ID NO.: 22)
FGGFL	(SEQ ID NO.: 8)	fGGFL	(SEQ ID NO.: 23)
YPGFL	(SEQ ID NO.: 12)	yGGFL	(SEQ ID NO.: 24)
LAGFL	(SEQ ID NO.: 9)	faGFL	(SEQ ID NO.: 25)
FAGFL	(SEQ ID NO.: 10)	wGGFL	(SEQ ID NO.: 26)
WGGFL	(SEQ ID NO.: 11)	yaGFL	(SEQ ID NO.: 27)
		fpGFL	(SEQ ID NO.: 28)
		waGFL	(SEQ ID NO.: 29)

Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (pages i - xi).

REMARKS

Amendments to the Specification

The specification has been amended to insert SEQ ID Nos in accordance with the Sequence Listing submitted concurrently herewith.

Proposed Drawing Correction

Figure 22A is being submitted concurrently herewith to incorporate the SEQ ID Nos in accordance with the Sequence Listing. No new matter has been added.

Information Disclosure Statement

A Third Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Entry of the SIDS is respectfully requested.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Pamela A. Torpey (45,736) for
Lisa M. Treannie
Registration No. 41,368
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133

Date: August 1, 2002

MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Please replace the paragraph at page 13, lines 9 through 12, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Fig. 18 illustrates fluorescence of a slide with the peptide YGGFL (SEQ ID NO.: 1) on selected regions of its surface which has been exposed to labeled Herz antibody specific for this sequence.

Please replace the paragraph at page 13, lines 13 through 19, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Figs. 19A to 19D illustrate formation of and a fluorescence plot of a slide with a checkerboard pattern of YGGFL (SEQ ID NO.: 1) and GGFL (SEQ ID NO.: 2) exposed to labeled Herz antibody. Fig. 19C illustrates a 500x500 μm mask which has been focused on the substrate according to Fig. 12A while Fig. 19D illustrates a 50x50 μm mask placed in direct contact with the substrate in accord with Fig. 12B.

Please replace the paragraph at page 13, lines 20 through 21, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Fig. 20 is a fluorescence plot of YGGFL (SEQ ID NO.: 1) and PGGFL (SEQ ID NO.: 3) synthesized in a 50 μ m checkerboard pattern.

Please replace the paragraph at page 13, lines 22 through 23, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Fig. 21 is a fluorescence plot of YPGGFL (SEQ ID NO.: 4) and YGGFL (SEQ ID NO.: 1) synthesized in a 50 μ m checkerboard pattern.

Please replace the paragraph at page 56, line 23 through page 57 line 2, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

H. Attachment of YGGFL (SEQ ID NO.: 1) and Subsequent Exposure to Herz Antibody and Goat Antimouse

In order to establish that receptors to a particular polypeptide sequence would bind to a surface-bound peptide and be detected, Leu enkephalin was coupled to the surface and recognized by an antibody. A slide was derivatized with 0.1% amino propyl-triethoxysilane and protected with NVOC. A 500 μ m checkerboard mask was used to expose the slide in a flow cell using backside contact printing. The Leu enkephalin sequence (H₂N-tyrosine, glycine, glycine, phenylalanine, leucine-CO₂H, otherwise referred to herein as YGGFL (SEQ ID NO.: 1)) was attached via its carboxy end to the exposed amino groups on the surface of the slide. The peptide was added in DMF solution with the BOP/HOBT/DIEA coupling reagents and recirculated through the flow cell for 2 hours at room temperature.

Please replace the paragraph at page 57, lines 23 through 29, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

I. Monomer-by-Monomer Formation of YGGFL (SEQ ID NO.: 1) and Subsequent Exposure to Labeled Antibody

Monomer-by-monomer synthesis of YGGFL (SEQ ID NO.: 1) and GGFL (SEQ ID NO.: 2) in alternate squares was performed on a slide in a checkerboard pattern and the resulting slide was exposed to the Herz antibody. This experiment and the results thereof are illustrated in Figs. 19A, 19B, 19C, and 19D.

Please replace the paragraph at page 58, lines 9 through 20, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

As shown in Fig. 19B, alternating regions of the slide were then illuminated using a projection print using a 500x500 μm checkerboard mask; thus, the amino of group of glycine was exposed only in the lighted areas. When the next coupling chemistry step was carried out, NVOC-tyrosine was added, and it coupled only at those spots which had received illumination. The entire slide was then illuminated to remove all the NVOC groups, leaving a checkerboard of YGGFL (SEQ ID NO.: 1) in the lighted areas and in the other areas, GGFL (SEQ ID NO.: 2). The Herz antibody (which recognizes [the] YGGFL (SEQ ID NO.: 1), but not GGFL (SEQ ID NO.: 2)) was then added, followed by goat anti-mouse fluorescein conjugate.

Please replace the paragraph at page 58, lines 21 through 30, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

The resulting fluorescence scan is shown in Fig. 19C, and the color coding for the fluorescence intensity is again given on the right. Dark areas contain the tetrapeptide GGFL (SEQ ID NO.: 2), which is not recognized by the Herz antibody (and thus there is no binding of the goat anti-mouse antibody with fluorescein conjugate), and in the red areas YGGFL (SEQ ID NO.: 1) is present. The YGGFL (SEQ ID NO.: 1) pentapeptide is recognized by the Herz antibody and, therefore, there is antibody in the lighted regions for the fluorescein-conjugated goat anti-mouse to recognize.

Please replace the paragraph at page 59, lines 2 through 10, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

J. Monomer-by-Monomer Synthesis of YGGFL (SEQ ID NO.: 1) and PGGFL (SEQ ID NO.: 3)

A synthesis using a 50 μ m checkerboard mask similar to that shown in Fig. 19 was conducted. However, P was added to the GGFL (SEQ ID NO.: 2) sites on the substrate through an additional coupling step. P was added by exposing protected GGFL (SEQ ID NO.: 2) to light through a mask, and [subsequence] subsequent exposure to P in the manner set forth above. Therefore, half of the regions on the substrate contained YGGFL (SEQ ID NO.: 1) and the remaining half contained PGGFL (SEQ ID NO.: 3).

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Please replace the paragraph at page 59, lines 17 through 26, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

K. Monomer-by-Monomer Synthesis of YGGFL (SEQ ID NO.: 1) and YPGGFL (SEQ ID NO.: 4)

In order to further demonstrate the operability of the invention, a 50 μ m checkerboard pattern of alternating YGGFL (SEQ ID NO.: 1) and YPGGFL (SEQ ID NO.: 4) was synthesized on a substrate using techniques like those set forth above. The resulting fluorescence plot is provided in Fig. 21. Again, it is seen that the antibody is clearly able to recognize the YGGFL (SEQ ID NO.: 1) sequence and does not bind significantly at the YPGGFL (SEQ ID NO.: 4) regions.

Please replace the paragraph at page 60, lines 10 through 22, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Fig. 23 is a fluorescence plot of the first slide, which contained only L amino acids. Red indicates strong binding (149,000 counts or more) while black indicates little or no binding of the Herz antibody (20,000 counts or less). The bottom right-hand portion of the slide appears “cut off” because the slide was broken during processing. The sequence YGGFL (SEQ ID NO.: 1) is clearly most strongly recognized. The sequences YAGFL (SEQ ID NO.: 5) and YSGFL (SEQ ID NO.: 6) also exhibit strong recognition of the antibody. By contrast, most of the remaining sequences show little or no binding. The four duplicate portions of the slide are extremely consistent in the amount of binding shown therein.

Please replace the paragraph at page 60, lines 23 through 28, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Fig. 24 is a fluorescence plot of the second slide. Again, strongest binding is exhibited by the YGGFL (SEQ ID NO.: 1) sequence. Significant binding is also detected to YaGFL (SEQ ID NO.: 20), YsGFL (SEQ ID NO.: 21), and YpGFL (SEQ ID NO.: 22). The remaining sequences show less binding with the antibody. Note the low binding efficiency of the sequence yGGFL (SEQ ID NO.: 24).

Please replace the table at page 61, lines 1 through 17, with the below table marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Table 6
Apparent Binding to Herz Ab

<u>L-a.a. Set</u>		<u>D-a.a. Set</u>	
YGGFL	<u>(SEQ ID NO.: 1)</u>	YGGFL	<u>(SEQ ID NO.: 1)</u>
YAGFL	<u>(SEQ ID NO.: 5)</u>	YaGFL	<u>(SEQ ID NO.: 20)</u>
YSGFL	<u>(SEQ ID NO.: 6)</u>	YsGFL	<u>(SEQ ID NO.: 21)</u>
LGGFL	<u>(SEQ ID NO.: 7)</u>	YpGFL	<u>(SEQ ID NO.: 22)</u>
FGGFL	<u>(SEQ ID NO.: 8)</u>	fGGFL	<u>(SEQ ID NO.: 23)</u>
YPGFL	<u>(SEQ ID NO.: 12)</u>	yGGFL	<u>(SEQ ID NO.: 24)</u>
LAGFL	<u>(SEQ ID NO.: 9)</u>	faGFL	<u>(SEQ ID NO.: 25)</u>
FAGFL	<u>(SEQ ID NO.: 10)</u>	wGGFL	<u>(SEQ ID NO.: 26)</u>
WGGFL	<u>(SEQ ID NO.: 11)</u>	yaGFL	<u>(SEQ ID NO.: 27)</u>
		fpGFL	<u>(SEQ ID NO.: 28)</u>

Please replace the paragraph at page 185, lines 18 through 33, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

9. attachment of YGGFL (SEQ ID NO.: 1) and subsequent exposure to herz antibody and goat antimouse antibody

In order to establish that receptors to a particular polypeptide sequence would bind to a surface-bound peptide and be detected, Leu enkephalin was coupled to the surface and recognized by an antibody. A slide was derivatized with 0.1% amino propyl-triethoxysilane and protected with NVOC. A 500 μ m checkerboard mask was used to expose the slide in a flow cell using backside contact printing. The Leu enkephalin sequence (H₂N-tyrosine, glycine, glycine, phenylalanine, leucine-COOH, otherwise referred to herein as YGGFL (SEQ ID NO.: 1)) was attached via its carboxy end to the exposed amino groups on the surface of the slide. The peptide was added in DMF solution with the BOP/HOBT/DIEA coupling reagents and recirculated through the flow cell for 2 hours at room temperature.

Please replace the paragraph at page 186, lines 15 through 20, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

10. monomer-by-monomer formation of YGGFL (SEQ ID NO.: 1) and subsequent exposure to labeled antibody

Monomer-by-monomer synthesis of YGGFL (SEQ ID NO.: 1) and GGFL (SEQ ID NO.: 2) in alternate squares was performed on a slide in a checkerboard pattern and the resulting slide was exposed to the Herz antibody.

Please replace the paragraph at page 186, line 36 through page 187 line 7, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Alternating regions of the slide were then illuminated using a projection print using a 500x500 μm checkerboard mask; thus, the amino of group of glycine was exposed only in the lighted areas. When the next coupling chemistry step was carried out, NVOC-tyrosine was added, and it coupled only at those spots which had received illumination. The entire slide was then illuminated to remove all the NVOC groups, leaving a checkerboard of YGGFL (SEQ ID NO.: 1) in the lighted areas and in the other areas, GGFL (SEQ ID NO.: 2). The Herz antibody (which recognizes [the] YGGFL (SEQ ID NO.: 1), but not GGFL (SEQ ID NO.: 2)) was then added, followed by goat anti-mouse fluorescein conjugate.

Please replace the paragraph at page 187, lines 8 through 15, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

The resulting fluorescence scan showed dark areas contain the tetrapeptide GGFL (SEQ ID NO.: 2), which is not recognized by the Herz antibody (and thus there is no binding of the goat anti-mouse antibody with fluorescein conjugate), and red areas in which YGGFL (SEQ ID NO.: 1) was present. The YGGFL (SEQ ID NO.: 1) pentapeptide is recognized by the Herz antibody and, therefore, there is antibody in the lighted regions for the fluorescein-conjugated goat anti-mouse to recognize.

Please replace the paragraph at page 187, lines 23 through 31, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

11. monomer-by-monomer synthesis of YGGFL (SEQ ID NO.: 1) and PGGFL (SEQ ID NO.: 3)

A synthesis using a 50 μ m checkerboard mask was conducted. However, P was added to the GGFL (SEQ ID NO.: 2) sites on the substrate through an additional coupling step. P was added by exposing protected GGFL (SEQ ID NO.: 2) to light through a mask, and subsequence exposure to P in the manner set forth above. Therefore, half of the regions on the substrate contained YGGFL (SEQ ID NO.: 1) and the remaining half contained PGGFL (SEQ ID NO.: 3).

Please replace the paragraph at page 188, lines 1 through 9, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

12. monomer-by-monomer synthesis of YGGFL (SEQ ID NO.: 1) and YPGGFL (SEQ ID NO.: 4)

In order to further demonstrate the operability of the invention, a 50 μ m checkerboard pattern of alternating YGGFL (SEQ ID NO.: 1) and YPGGFL (SEQ ID NO.: 4) was synthesized on a substrate using techniques like those set forth above. The resulting fluorescence plot showed that the antibody is clearly able to recognize the YGGFL (SEQ ID NO.: 1) sequence and did not bind significantly at the YPGGFL (SEQ ID NO.: 4) regions.

Please replace the paragraph at page 188, lines 27 through 36, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

-X-

A fluorescence plot of the first slide, which contained only L amino acids showed red areas (indicating strong binding, i.e., 149,000 counts or more) and black areas (indicating little or no binding of the Herz antibody, i.e., 20,000 counts or less). The sequence YGGFL (SEQ ID NO.: 1) was clearly most strongly recognized. The sequences YAGFL (SEQ ID NO.: 5) and YSGFL (SEQ ID NO.: 6) also exhibited strong recognition of the antibody. By contrast, most of the remaining sequences show little or no binding. The four duplicate portions of the slide were extremely consistent in the amount of binding shown therein.

Please replace the paragraph at page 188, line 37 through page 189 line 3, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

A fluorescence plot of the D-amino acid slide indicated that strongest binding was exhibited by the YGGFL (SEQ ID NO.: 1) sequence. Significant binding was also detected to YaGFL (SEQ ID NO.: 20), YsGFL (SEQ ID NO.: 21), and YpGFL (SEQ ID NO.: 22). The remaining sequences showed less binding with the antibody. Low binding efficiency of the sequence yGGFL (SEQ ID NO.: 24) was observed.

Please replace the table at page 190, lines 1 through 17, with the below table marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Table 6
Apparent Binding to Herz Ab

<u>L-a.a. Set</u>		<u>D-a.a. Set</u>	
YGGFL	<u>(SEQ ID NO.: 1)</u>	YGGFL	<u>(SEQ ID NO.: 1)</u>
YAGFL	<u>(SEQ ID NO.: 5)</u>	YaGFL	<u>(SEQ ID NO.: 20)</u>
YSGFL	<u>(SEQ ID NO.: 6)</u>	YsGFL	<u>(SEQ ID NO.: 21)</u>
LGGFL	<u>(SEQ ID NO.: 7)</u>	YpGFL	<u>(SEQ ID NO.: 22)</u>

FGGFL	<u>(SEQ ID NO.: 8)</u>	fGGFL	<u>(SEQ ID NO.: 23)</u>
YPGFL	<u>(SEQ ID NO.: 12)</u>	yGGFL	<u>(SEQ ID NO.: 24)</u>
LAGFL	<u>(SEQ ID NO.: 9)</u>	faGFL	<u>(SEQ ID NO.: 25)</u>
FAGFL	<u>(SEQ ID NO.: 10)</u>	wGGFL	<u>(SEQ ID NO.: 26)</u>
WGGFL	<u>(SEQ ID NO.: 11)</u>	yaGFL	<u>(SEQ ID NO.: 27)</u>
		fpGFL	<u>(SEQ ID NO.: 28)</u>
		waGFL	<u>(SEQ ID NO.: 29)</u>
